--13. A method of repairing a cartilage and bone fracture or defect in a warm-blooded animal comprising administering locally to a warm-blooded animal a composition of claim 12 at the site of a bone or cartilage fracture or defect.--

Claims 8, 10 and 11, line 1 of each, change "7" to --13--

REMARKS

Reconsideration of this application is requested in view of the amendments to the claims and the remarks presented herein. Entry of the amendment is requested under the provisions of Rule 116 as it puts the application in condition for allowance or in better condition for appeal.

Applicants' attorney wishes to thank the Examiner for the courtesies extended to him at the interview on July 12, 2000 when the formal rejection was discussed.

The claims in the application are claims 2 to 5 and 8 to 13, all other claims having been cancelled.

Claims 2 to 5 and 8 to 13 were rejected under 35 USC 112, first paragraph, as containing new matter in the temperature limitation and in the expression "agent".

Applicants respectfully traverse this ground of rejection

since the amended claims clearly do not contain new matter. With respect to the temperature limitation of 1 to 30°C, the Examiner's attention is directed to line 8 of page 4 wherein this limitation is recited. With respect to the term "agent", the same has been changed to "protein" as suggested by the Examiner. Therefore, the claims do not contain new matter and withdrawal of this objection is requested.

Claims 2 to 5 and 7 to 12 were rejected under 35 USC 112, second paragraph, as being indefinite. The Examiner objected to claim 12 as being incorrect in the glycol and in the molecular weight of 900 to 4,000 and in the term "agent". The Examiner also objected to the expression "repairing" or "repairing material" as not finding antecedent basis in claim 12 (sic 1). Claims 4 and 5 were rejected as being indefinite in the term "in either" and claim 5 was rejected as being indefinite in the term "treating".

Applicants respectfully traverse these grounds of rejection since the amended claims are believed to properly define the invention. The spelling error in the expression "polyoxyethylene-polypropylene glycol" has been corrected and the molecular weight is correct as can be seen from the last line of page 4. The term "agent" has been replaced by the term "protein" as suggested by the Examiner. Claim 12 has been amended to provide antecedent basis for the term "repairing material". Claims 4 and 5 are not indefinite in the term "in either" since this was corrected in the

preliminary amendment, a copy of which is enclosed herewith for the Examiner's convenience. Claim 12 recites that the composition is collagen-free which is supported by the paragraph bridging page 2 and 3 and lines 20 and 21 of page 3. Claim 7 has been rewritten as claim 13 to more clearly define the claimed method. Therefore, the amended claims are believed to properly define the invention and withdrawal of these grounds of rejection is requested.

Claim 2 to 5 and 12 were rejected under 35 USC 102 as being anticipated by or under 35 USC 103 as being obvious over WO 94/1483. The Examiner refers to therapeutic compositions containing a polyoxyetheylene-polyoxypropylene in lines 15 and 16 of page 3 and a bone morphogenic protein in line 33 of page 10 and that the composition is in aqueous solution which is injectable and remains in liquid form at body temperature and refers to pages 4 and 5. The molecular weight for the polymer can be adjusted depending upon the desired release rate with the Examiner referring to the first paragraph of page 9 and the Examiner deems that the invention would be obvious if not anticipated.

Claims 2 to 5 and 7 to 12 were rejected under 35 USC 103 as being obvious over the said reference taken in view of the Japanese '431 or the Ron et al reference for reasons of record. The Examiner states that Applicants have not clearly and specifically pointed out the basis for the amendatory materials and noted that there was a typographical error in claim 2. With respect to the

paragraph bridging pages 6 and 7, the Examiner is of the opinion that this did not support the temperature range of 1 to 30°C or the molecular weight of 900 to 4,000. For some reason, the Examiner deemed that line 13 of page 7 was erroneous.

Applicants respectfully traverse these grounds of rejection since WO 94/1484 does not anticipate or render the invention obvious whether taken alone or in view of the secondary references. As pointed out at the interview, there is some error in the Examiner's statements since none of the page references and lines referred to in the office action correspond to what the Examiner says. For instance, lines 15 and 16 have nothing to do whatsoever with a polyoxyethylene-polyoxypropylene but merely, talks about varying the method so that the reaction between the naturally occurring polymer and the synthetic polymer occurs in situ. The same is true with respect to line 33 of page 10 and the first paragraph of page 9. Moreover, the reference to pages 4 and 5 does not support the Examiner's position.

Basically, the primary reference wishes to produce a non-immugenic conjugate formed by covalently bonding a biologically inactive natural polymer or a derivative thereof to a synthetic hydrophilic polymer by specific types of chemical bonds. The preferred conjugate is PEG and collagen and Applicants' claims has been amended to point out that they wish to have a collagen free composition. This is supported by the paragraph bridging pages 2

and 3 wherein it is stated that collagen is a known carrier for bone morphogenic protein but the collagen presently available has varying properties such as molecular weights, amino acid composition and a moisture holding property. In addition, it also has side effects such as anti-genicity which cannot be completely eliminated even when atelocollagen is used. Further, on page 3 beginning at line 20, it is deemed that one of the objects of the invention is to avoid the prior art disadvantages such as that obtained with collagen.

It should be noted that Applicants' invention is directed to a) collagen free aqueous solution of a polyoxyethylene-polyoxypropylene glycol and an effective amount of a bone morphogenic protein. The molecular weight of the polyoxypropylene glycol in the composition is between 900 and 4,000 and the ethylene oxide portion is between 5 to 90% by weight of the molecule. Applicants' compositions have the advantage that they are in aqueous solution at 1 to 30°C and when administered at the point of bone fracture, it gelatinizes at body temperature which permits the administration at the point where needed. This is in no way taught or suggested by the WO 94/1483 patent and therefore, withdrawal of these grounds of rejection is requested.

In view of the amendments to the specification and claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
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CAM:ds
Encl.: Copy of preliminary amendment
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